FIGURE 1A

Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I					
Rhodopsin like					
	•Amine				
	•Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors				
	•Alpha Adrenoceptors	6	Brain, Kidney, Lung	Gluconeogenesis	Diabetes, Cardiovascular
	•Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	•Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	• Peptide				
	•Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	•Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	•Orexin	2	Brain	Fat Metabolism	Obesity
	•Nociceptin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic
	•Opioid	3	Brain,	CNS	Depression, Analgesic
	•Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Tachykinin (Substance P, NKA_1)	3	Brain Nerves	Neurohormone	Depression, Analgesic

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FIGURE 1B

•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
•Hormone protein				
•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
•Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Infertility
•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•(Rhod)opsin				
•Opsin	5	Eye	Photoreception	Ophthalmic Diseases
•Olfactory	4(~1000)	Nose	Smell	Olfactory Diseases
•Prostanoid				
•Prostaglandin	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
•Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Nucleotide-like				
•Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Purinoceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
•Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone- inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Class II				
Secretin like				
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/urocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular

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FIGURE 1C

	•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis	Cardiovascular, Diabetes, Obesity
	•Growth hormone-releasing hormone	1	Brain	Neuroendocrine	Growth Regulation
	•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
	•PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
	•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•ClassIII					
	•Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
	•$GABA_B$	1	Brain	Neurotransmitter	Mood Disorders
	•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors

REPLACEMENT SHEET

FIGURE 2A

G protein-coupled receptors:
(Division into Class A
Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyaf riqkfrvtfl kiwndhfrcq pappidedlp eerpdd
Class A

2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiypc sskefkrafv rilgcqcrgr grrrrrrrr lggcaytyrp wtrggslers qsrkdsldds gsclsgsqrt lpsaspspgy lgrgapppve lcafpewkap gallslpape ppgrrgrhds gplftfkllt epespgtdgg asnggceaaa dvangqpgfk snmplapgqf
Class A

3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviytifn hdfrrafkki lcrgdrkriv
Class A

4. **alpha-2B-adrenergic receptor** - human. ACCESSION A37223
npviytifn qdfrrafrri lcrpwtqtaw
Class A

5. **alpha-2C-adrenergic receptor** - human. ACCESSION A31237
npviytvfn qdfrpsfkhi lfrrrrrgfr q
Class A

6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiycrs pdfrkafqgl lccarraarr rhathgdrpr asgclarpgp ppspgaasdd ddddvvgatp parllepwag cnggaaadsd ssldepcrpg faseskv
Class A

7. **beta-2 adrenergic receptor**. ACCESSION P07550
npliycrsp dfriafqell clrrsslkay gngyssngnt 361 geqsgyhveq ekenkllced lpgtedfvgh qgtvpsdnid sqgrncstnd sll
Class A

8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npii yafnadfrka fstllgcyrl cpatnnaiet vsinnngaam fsshheprgs iskecnlvyl iphavgssed lkkeeaagia rpleklspal svildydtdv slekiqpitq ngqhpt
Class A

9. **D(2) dopamine receptor.** ACCESSION P14416
npiiyttfn iefrkaflki lhc
Class A

REPLACEMENT SHEET

FIGURE 2B

10. **d3 dopamine receptor** - human. ACCESSION G01977
np viyttfnief rkaflkilsc
Class A

11. **dopamine receptor D4** - human. ACCESSION DYHUD4
npviytv fnaefrnvfr kalracc
Class A

12. **dopamine receptor D5** - human. ACCESSION DYHUD5
npviya fnadfqkvfa qllgcshfcs rtpvetvnis nelisynqdi vfhkeiaaay ihmmpnavtp gnrevdndee egpfdrmfqi yqtspdgdpv aesvweldce geisldkitp ftpngfh
Class A

13. **muscarinic acetylcholine receptor M1** [Homo sapiens]. ACCESSION NP_000729
npmcyal cnkafrdtfr llllcrwdkr rwrkipkrpg svhrtpsrqc
Class A

14. **muscarinic acetylcholine receptor M2** [Homo sapiens]. ACCESSION NP_000730
npacy alcnatfkkt fkhllmchyk nigatr
Class A

15. **muscarinic acetylcholine receptor M3 [Homo sapiens].** ACCESSION NP_000731
n pvcyalcnkt frttfkmlll cqcdkkkrrk qqyqqrqsvi fhkrapeqal
Class A

16. **muscarinic acetylcholine receptor M4** [Homo sapiens]. ACCESSION NP_000732
npa cyalcnatfk ktfrhlllcq yrnigtar
Class A

17. **m5 muscarinic receptor.** locus HUMACHRM ACCESSION AAA51569
npicyalcnr tfrktfkmll lcrwkkkkve eklywqgnsk lp
Class A

18. **5-hydroxytryptamine (serotonin) receptor 1A** [Homo sapiens]. ACCESSION BAA90449
npviy ayfnkdfqna fkkiikckf
Class A

19. **5-hydroxytryptamine (serotonin) receptor 1B** [Homo sapiens]. ACCESSION BAA94455
npiiyt msnedfkqaf hklirfkcts
Class A

20. **5-hydroxytryptamine (serotonin) receptor 1E** [Homo sapiens]. ACCESSION BAA94458
n pllytsfned fklafkklir cre
Class A

REPLACEMENT SHEET

FIGURE 2C

21. **OLFACTORY RECEPTOR 6A1**. ACCESSION O95222
npiiyclrnq evkralccil hlyqhqdpdp kkgsrnv
Class A

22. **OLFACTORY RECEPTOR 2C1**. ACCESSION O95371
npliy tlrnmevkga lrrllgkgre vg
Class A

23. **angiotensin receptor 1 [Homo sapiens].** ACCESSION NP_033611
npl fygflgkkfk ryflqllkyi ppkakshsnl *s*fkm*s*fl*s*yr psdnv*sss*tk kpapcfeve
Class B

24. **angiotensin receptor 2** [Homo sapiens]. ACCESSION NP_000677
npflycf vgnrfqqklr svfrvpitwl qgkresmscr k*sss*lremet fvs
Class B

25. **interleukin 8 receptor beta (CXCR2)** [Homo sapiens]. ACCESSION NM_001557
NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL
Class B

26. **cx3c chemokine receptor 1** (cx3cr1) (fractalkine receptor)
ACCESSION P49238
np liyafagekf rrylyhlygk clavlcgrsv hvdf*sss*e*s*q rsrhg*s*v*l*s*s* nftyhtsdgd allll
Class B

27. **neurotensin receptor - human.** ACCESSION S29506
n pilynlvsan frhiflatla clcpvwrrrr krpafsrkad *s*v*ss*nhf*l*s*s* natretly
Class B

28. **SUBSTANCE-P RECEPTOR (SPR)** (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103
npiiyccInd rfrlgfkhaf rccpfisagd yeglemkstr ylqtqgsvyk vsrle*tt*i*st*vvgaheeepe dgpka*t*p*ss*l
dlt*s*nc*ss*r*s* d*s*ktmte*s*fs f*ss*nvls
Class B

29. **vasopressin receptor type 2** [Homo sapiens]. ACCESSION AAD16444
npwiyasfss svsselrsll ccargrtpps lgpqde*sctt* a*sss*lakd*ts s*
Class B

30. **thyrotropin-releasing hormone receptor** - human. ACCESSION JN0708
npviy nlmsqkfraa frklcnckqk ptekpanysv alnysvikes dhf*st*elddi *tvtdtyls at* kvsfddtcla sevsfsqs
Class B

31. **oxytocin receptor - human.** ACCESSION A55493
npwiym lftghlfhel vqrflccsas ylkgrrlget *s*a*s*kk*s*n*sss* fvl*s*hr*sss*q rsc*s*qpsta
Class B

REPLACEMENT SHEET

FIGURE 2D

32. **neuromedin U receptor [Homo sapiens].** ACCESSION AAG24793
npvlyslmssrfretfqealclgacchrlrprhsshslsrmttgstlcdvgslgswvhplagndgpeaqqetdps
Class B

33. **gastrin receptor.** ACCESSION AAC37528
nplvy cfmhrrfrqa cletcarccp rpprarpral pdedppt*p*si a*s*l*s*rl*s*y*tt is*flgpg
Class B

34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541
nplv yalasrhfra rfrrlwpcgr rrrhrarral rrvrpassgp pgcpgdarps grllagggqg pepregpvhg geaargpe
Class A

35. **edg-1** - human. ACCESSION A35300
npiiy tltnkemrra firimsckc psgdsagkfk rpiiagmefs rsksdnsshp 361 qkdegdnpet imssgnvnss s
Class A

36. **central cannabinoid receptor** [Homo sapiens]. ACCESSION NP_057167
npiiyalr skdlrhafrs mfpscegtaq pldnsmgdsd clhkhannaa svhraaesci kstvkiakvt msvstdtsae al
Class A

37. **delta opioid receptor** - human. ACCESSION I38532
npvlyaf ldenfkrcfr qlcrkpcgrp dpssfsrpre atarervtac tpsdgpgggr aa
Class A

38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085
dpfvyyfvshdfrdhaknallcrsvrtvkqmqvsltskkhsrksssyssssttvktsy
Class A

39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM_012685
NGEVQAELRRKWRRWHLQGVLGW**S**S**K**S**Q**HPWGGSNGA**T**C**S**TQVSMLTRVSPSARR
SSSFQAEVSLV
Class B

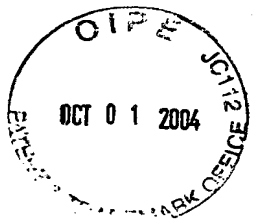

FIGURE 3A

Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):

gcccggggacgcaccccacccagcctgggtccccaagatgagtcctgcaccaccgccagctcct ccctggccaaggacacttcatcgtga

FIGURE 3B

PCR amplified human V2R DNA fragment:

gcggccgcacggggacgcaccccacccagcctgggtccccaagatgagtcctgcaccaccgcc agctcctccctggccaaggacacttcatcgtgaagatctccgcggtctaga

*Additions and changes to the V2R DNA are underlined.

*The Sma I (cccggg) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

FIGURE 4A

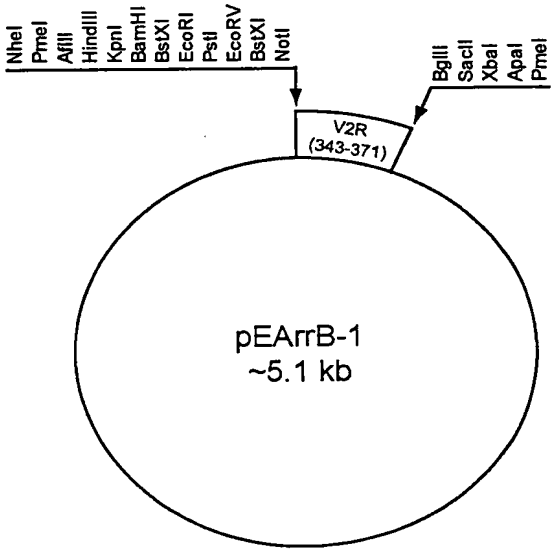

FIGURE 4B

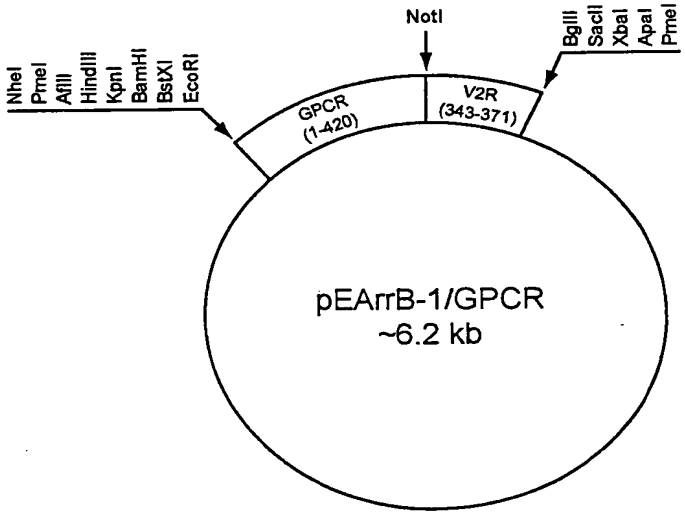

FIGURE 4C

...AAARGRTPPSLGPQDESCTTASSSLAKDTSS

FIGURE 7B

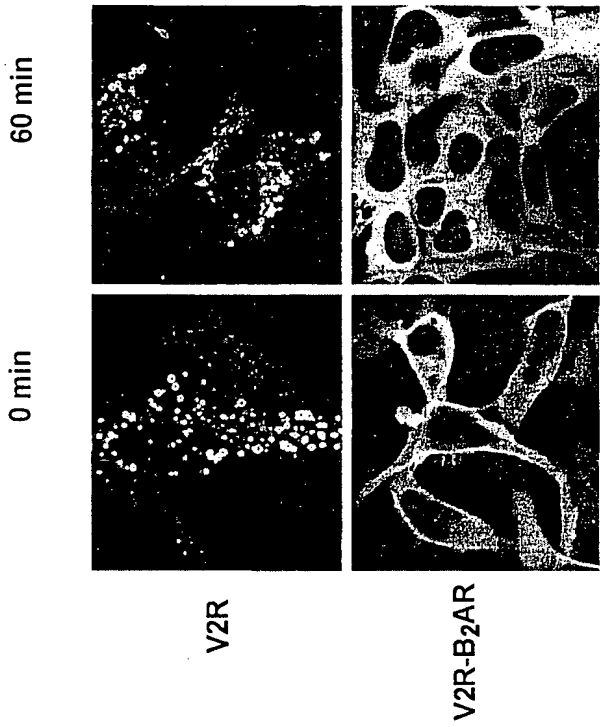

FIGURE 7A

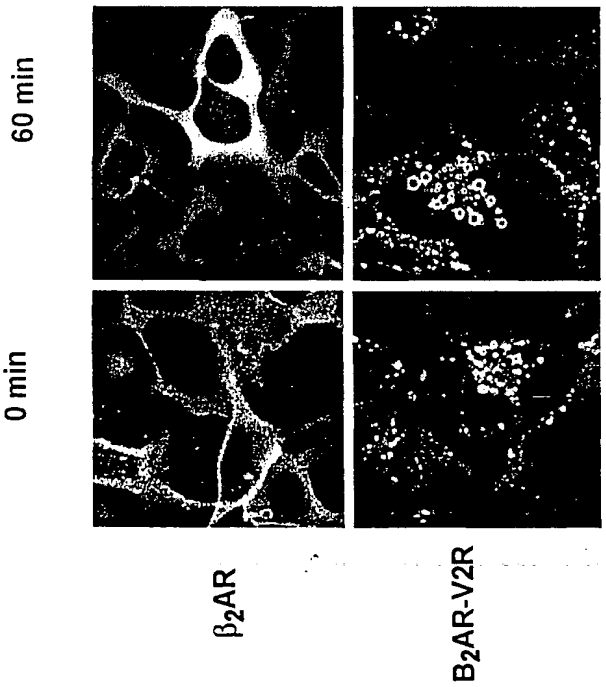

FIGURE 8A

1)	V2R	CARGRTPPSLGPQDESCTTASSSLAKDTSS
2)	V2R-S362X	CARGRTPPSLGPQDESCTTA
3)	V2R-SSSTSS/AAAAAA	CARGRTPPSLGPQDESCTTAAAALAKDAAA
4)	V2R-TSS/AAA	CARGRTPPSLGPQDESCTTASSSLAKDAAA
5)	V24-SSS/AAA	CARGRTPPSLGPQDESCTTAAAALAKDTSS
6)	β_2AR-V2R-SSS/AAA	CARGRTPPSLGPQDESCTTAAAALAKDTSS
7)	β_2AR	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP-GTEDFVGHQGTVPSDNIDSQGRNCSTNDSLL
8)	β_2AR413-V2R10	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP-GTEDFVGHQGTVPSDNIDSQGRNCSTNDSLLSSSLAKDTSS
9)	β_2AR360-V2R10	CLRRSSLKAYGNGYSSNGNTSSSLAKDTSS

FIGURE 8B

```
V2R      NPWIYASFSSSVSSELRSLLCCARGRTPPSLGPQDESCTTASSSLAKDTSS
AAA-1    ------------------------------------------AAA-------
AAA-2    -------------------------------------------------AAA

NTR-1    NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNSMSSNHAFSTSATRETLY
AMAA     ----------------------------------------A-AA--------------
AAA      -------------------------------------------------AAA-------

OTR      NPWIYMLFTGHLFHELVQRFLCCSASYLKGRRLGETSASKKSNSSSFVLSHRSSSQRSCSQPSTA
AAAA     ---------------------------------AAAA--------------------------
AAA-1    ------------------------------------------AAA--------------------
AAA-2    ---------------------------------------------------AAA-----------
```

REPLACEMENT SHEET

FIGURE 8C


```
SPR     NPIIYCCLNDRFRLGFKHAFRCCPFISAGDYEGLEMKSTRYLQTQGVYKVSRLETTISTVVGAHEEEPEDGPKATPSSLKLTSNCSSRSDSKTMTESFSFSSNVLS
383X    ----------------------------------------------------------------X
355X    ------------------------------------------------------------------X
325X    ----------X-------------------AA-AA-----------------------------------
AAIAA   ------------------------------------------------------A-AA-------------
APAA    ------------------------------------------------------A-AA-------------
```

FIGURE 9A

Amino Acid Sequence of the Wild-Type Receptors

Amino acid sequence of the wild-type V2R

MLMASTTSAVPGHPSLPSLPSNSSQERPLDTRDPLLARAELALLSIVFVAVALSNGLVLAA
LARRGRRGHWAPIHVFIGHLCLADLAVALFQVLPQLAWKATDRFRGPDALCRAVKYLQMVG
MYASSYMILAMTLDRHRAICRPMLAYRHGSGAHWNRPVLVAWAFSLLLSLPQLFIFAQRNV
EGGSGVTDCWACFAEPWGRRTYVTWIALMVFVAPTLGIAACQVLIFREIHASLVPGPSERP
GGRRRGRRTGSPGEGAHVSAAVAKTVRMTLVIVVVYVLCWAPFFLVQLWAAWDPEAPLEGA
PFVLLMLLASLNSCTNPWIYASFSSSVSSELRSLLCC**ARGRTPPSLGPQDESCTTASSSLA**
KDTSS
(Seq.ID No.1)

FIGURE 9B

Amino acid sequence of the wild-type β_2AR

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVLVITAIAKF
ERLQTVTNYFITSLACADLVMGLAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE
TLCVIAVDRYFAITSPFKYQSLLTKNKARVIILMVWIVSGLTSFLPIQMHWYRATHQEAIN
CYANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQN
LSQVEQDGRTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRK
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGY
HVEQEKENKLLCEDLPGTEDFVGHQGTVPSDNIDSQGRNCSTNDSLL
(Seq. ID No. 2)

FIGURE 9C

Amino Acid Sequence of the Chimeric Receptors

Amino acid sequence of the β_2AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVLVITAIAKF
ERLQTVTNYFITSLACADLVMGLAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE
TLCVIAVDRYFAITSPFKYQSLLTKNKARVIILMVWIVSGLTSFLPIQMHWYRATHQEAIN
CYANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQN
LSQVEQDGRTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRK
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLC**ARGRTPPSLGPQDESCTTASSSLAK**
DTSS
(Seq. ID No. 3)

*shown in bold are the amino acids that were moved to the β_2AR to increase its affinity for arrestin.

FIGURE 10A

Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLG
GNDSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTA
TNIYIFNLALADALATSTLPFQSVNYLMGTWPFGTILCKIVISIDYYNMFT
SIFTLCTMSVDRYIAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMF
MATTKYRQGSIDCTLTFSHPTWYWENLLKICVFIFAFIMPILIITVCYGLM
ILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVFIVCWTPIHIYVIIKALI
TIPETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENFKRCFREFC**AAARGR**
TPPSLGPQDESCTTASSSLAKDTSS
(Seq. ID No. 4)

FIGURE 10B

Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFR
HLRSKVTNFFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFD
IMCSTASILNLCVISVDRYWAISSPFQYERKMTPKAAFILISVAWTLSVLI
SFIPVQLSWHKAKPTWPLDGNFTSLEDTEDDNCDTRLSRTYAISSSLISFY
IPVAIMIVTYTSIYRIAQKQIRRISALERAAVHAKNCQTTAGNGNPVECAQ
SESSFKMSFKRETKVLKTLSVIMGVFVCCWLPFFISNCMVPFCGSEETQPF
CIDSITFDVFVWFGWANSSLNPIIYAFNADFQKAFSTLLGCYRLC**AAARGR**
TPPSLGPQDESCTTASSSLAKDTSS
(Seq. ID No. 5)

FIGURE 10C

Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector

MDVLSPGQGNNTTSPPAPFETGGNTTGISDVTVSYQVITSLLLGTLIFCAV
LGNACVVAAIALERSLQNVANYLIGSLAVTDLMVSVLVLPMAALYQVLNKW
TLGQVTCDLFIALDVLCCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRA
AALISLTWLIGFLISIPPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAF
YIPLLLMLVLYGRIFRAARFRIRKTVKKVEKTGADTRHGASPAPQPKKSVN
GESGSRNWRLGVESKAGGALCANGAVRQGDDGAALEVIEVHRVGNSKEHLP
LPSEAGPTPCAPASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILC
WLPFFIVALVLPFCESSCHMPTLLGAI
INWLGYSNSLLNPVIYAYFNKDFQNAFKKIIKCNFC**AAARGRTPPSLGPQD**
ESCTTASSSLAKDTSS
(Seq. ID No. 6)

FIGURE 10D

Amino acid sequence of the β3AR-V2R chimera expressed from the pEArrB-1/β3AR vector

MAPWPHENSSLAPWPDLPTLAPNTANTSGLPGVPWEAALAGALLALAVLAT
VGGNLLVIVAIAWTPRLQTMTNVFVTSLAAADLVMGLLVVPPAATLALTGH
WPLGATGCELWTSVDVLCVTASIETLCALAVDRYLAVTNPLRYGALVTKRC
ARTAVVLVWVVSAAVSFAPIMSQWWRVGADAEAQRCHSNPRCCAFASNMPY
VLLSSSVSFYLPLLVMLFVYARVFVVATRQLRLLRGELGRFPPEESPPAPS
RSLAPAPVGTCAPPEGVPACGRRPARLLPLREHRALCTLGLIMGTFTLCWL
PFFLANVLRALGGPSLVPGPAFLALNWLGYANSAFNPLIYCRSPDFRSAFR
RLLCRC**AAARGRTPPSLGPQDESCTTASSSLAKDTSS**
(Seq. ID No. 7)

FIGURE 10E

Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNYTGKLNISADKENSIKLTSVV
FILICCFIILENIFVLLTIWKTKKFHRPMYYFIGNLALSDLLAGVAYTANL
LLSGATTYKLTPAQWFLREGSMFVALSASVFSLLAIAIERYITMLKMKLHN
GSNNFRLFLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHKHYIL
FCTTVFTLLLLSIVILYCRIYSLVRTRSRRLTFRKNISKASRSSEKSLALL
KTVIIVLSVFIACWAPLFILLLLDVGCKVKTCDILFRAEYFLVLAVLNSGT
NPIIYTLTNKEMRRAFIRIMSCCKC**AAARGRTPPSLGPQDESCTTASSSLA**
KDTSS
(Seq. ID No. 8)

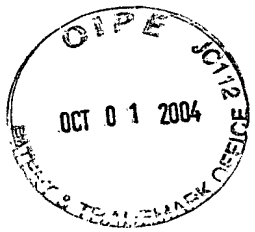

FIGURE 11A

Nucleotide sequence of the β2AR-V2R chimera

atggggcaacccgggaacggcagcgccttcttgctggcacccaatagaagccatgcgccggacc
acgacgtcacgcagcaaagggacgaggtgtgggtggtgggcatgggcatcgtcatgtctctcat
cgtcctggccatcgtgtttggcaatgtgctggtcatcacagccattgccaagttcgagcgtctg
cagacggtcaccaactacttcatcacttcactggcctgtgctgatctggtcatgggcctggcag
tggtgccctttggggccgcccatattcttatgaaaatgtggacttttggcaacttctggtgcga
gttttggacttccattgatgtgctgtgcgtcacggccagcattgagaccctgtgcgtgatcgca
gtggatcgctactttgccattacttcacctttcaagtaccagagcctgctgaccaagaataagg
cccgggtgatcattctgatggtgtggattgtgtcaggccttacctccttcttgcccattcagat
gcactggtaccgggccacccaccaggaagccatcaactgctatgccaatgagacctgctgtgac
ttcttcacgaaccaagcctatgccattgcctcttccatcgtgtccttctacgttcccctggtga
tcatggtcttcgtctactccagggtctttcaggaggccaaaaggcagctccagaagattgacaa
atctgagggccgcttccatgtccagaaccttagccaggtggagcaggatgggcggacggggcat
ggactccgcagatcttccaagttctgcttgaaggagcacaaagccctcaagacgttaggcatca
tcatgggcactttcaccctctgctggctgcccttcttcatcgttaacattgtgcatgtgatcca
ggataacctcatccgtaaggaagtttacatcctcctaaattggataggctatgtcaattctggt
ttcaatcccccttatctactgccggagcccagatttcaggattgccttccaggagcttctgtgc**g**
cccggggacgcaccccacccagcctgggtccccaagatgagtcctgcaccaccgccagctcctc
cctggccaaggacacttcatcgtga
(SEQ ID No. 9)

FIGURE 11B

Nucleotide sequence of the MOR-V2R chimera

atggacagcagcaccggcccagggaacaccagcgactgctcagacccccttagctcaggcaagtt
gctccccagcacctggctcctggctcaacttgtcccacgttgatggcaaccagtccgatccatg
cggtctgaaccgcaccgggcttggcgggaacgacagcctgtgccctcagaccggcagcccttcc
atggtcacagccattaccatcatggccctctactctatcgtgtgtgtagtgggcctcttcggaa
acttcctggtcatgtatgtgattgtaagatacaccaaaatgaagactgccaccaacatctacat
tttcaaccttgctctggcagacgccttagcgaccagtacactgccctttcagagtgtcaactac
ctgatgggaacatggcccttcggaaccatcctctgcaagatcgtgatctcaatagattactaca
acatgttcaccagcatattcaccctctgcaccatgagcgtggaccgctacattgctgtctgcca
cccagtcaaagccctggatttccgtaccccccgaaatgccaaaatcgtcaacgtctgcaactgg
atcctctcttctgccatcggtctgcctgtaatgttcatggcaaccacaaaatacaggcaggggt
ccatagattgcaccctcacgttctcccacccaacctggtactgggagaacctgctcaaaatctg
tgtctttatcttcgctttcatcatgccgatcctcatcatcactgtgtgttacggcctgatgatc
ttacgactcaagagcgttcgcatgctatcgggctccaaagaaaaggacaggaatctgcgcagga
tcacccggatggtgctggtggtcgtggctgtatttatcgtctgctggacccccatccacatcta
cgtcatcatcaaagcgctgatcacgattccagaaaccacatttcagaccgtttcctggcacttc
tgcattgctttgggttacacgaacagctgcctgaatccagttctttacgccttcctggatgaaa
acttcaagcgatgcttcagagagttctgc**gcggccgcacggggacgcaccccacccagcctggg**
tccccaagatgagtcctgcaccaccgccagctcctccctggccaaggacacttcatcgtga
(SEQ ID No. 10)

FIGURE 11C

Nucleotide sequence of the D1AR-V2R chimera

atggctcctaacacttctaccatggatgaggccgggctgccagcggagagggatttctcctttc
gcatcctcacggcctgtttcctgtcactgctcatcctgtccactctcctgggcaataccttgt
ctgtgcggccgtcatccggtttcgacacctgaggtccaaggtgaccaacttctttgtcatctct
ttagctgtgtcagatctcttggtggctgtcctggtcatgccctggaaagctgtggccgagattg
ctggcttttggccctttgggtccttttgtaacatctgggtagcctttgacatcatgtgctctac
ggcgtccattctgaacctctgcgtgatcagcgtggacaggtactgggctatctccagccctttc
cagtatgagaggaagatgaccccaaagcagccttcatcctgattagcgtagcatggactctgt
ctgtccttatatccttcatcccagtacagctaagctggcacaaggcaaagcccacatggccctt
ggatggcaattttacctccctggaggacaccgaggatgacaactgtgacacaaggttgagcagg
acgtatgccatttcatcgtccctcatcagcttttacatccccgtagccattatgatcgtcacct
acaccagtatctacaggattgcccagaagcaaaccggcgcatctcagccttggagagggcagca
gtccatgccaagaattgccagaccaccgcaggtaacgggaaccccgtcgaatgcgcccagtctg
aaagttcctttaagatgtccttcaagagggagacgaaagttctaaagacgctgtctgtgatcat
gggggtgtttgtgtgctgctggctccctttcttcatctcgaactgtatggtgcccttctgtggc
tctgaggagacccagccattctgcatcgattccatcaccttcgatgtgtttgtgtggtttgggt
gggcgaattcttccctgaaccccattatttatgcttttaatgctgacttccagaaggcgttctc
aaccctcttaggatgctacagactctgc**gcggccgcacggggacgcaccccacccagcctgggt**
ccccaagatgagtcctgcaccaccgccagctcctccctggccaaggacacttcatcgtga
(SEQ ID No. 11)

FIGURE 11D

Nucleotide sequence of the 5HT1AR-V2R chimera

atggatgtgctcagccctggtcagggcaacaacaccacatcaccaccggctccctttgagaccg
gcggcaacactactggtatctccgacgtgaccgtcagctaccaagtgatcacctctctgctgct
gggcacgctcatcttctgcgcggtgctgggcaatgcgtgcgtggtggctgccatcgccttggag
cgctccctgcagaacgtggccaattatcttattggctctttggcggtcaccgacctcatggtgt
cggtgttggtgctgcccatggccgcgctgtatcaggtgctcaacaagtggacactgggccaggt
aacctgcgacctgttcatcgccctcgacgtgctgtgctgcacctcatccatcttgcacctgtgc
gccatcgcgctggacaggtactgggccatcacggaccccatcgactacgtgaacaagaggacgc
cccggcgcgccgctgcgctcatctcgctcacttggcttattggcttcctcatctctatcccgcc
catgctgggctggcgcaccccggaagaccgctcggaccccgacgcatgcaccattagcaaggat
catggctacactatctattccacctttggagctttctacatcccgctgctgctcatgctggttc
tctatgggcgcatattccgagctgcgcgcttccgcatccgcaagacggtcaaaaaggtggagaa
gaccggagcggacacccgccatggagcatctcccgccccgcagcccaagaagagtgtgaatgga
gagtcggggagcaggaactggaggctgggcgtggagagcaaggctgggggtgctctgtgcgcca
atggcgcggtgaggcaaggtgacgatggcgccgccctggaggtgatcgaggtgcaccgagtggg
caactccaaagagcacttgcctctgcccagcgaggctggtcctacccctgtgcccccgcctct
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agacagtgaagacgctgggcatcatcatgggcaccttcatcctctgctggctgcccttcttcat
cgtggctcttgttctgcccttctgcgagagcagctgccacatgcccaccctgttgggcgccata
atcaattggctgggctactccaactctctgcttaaccccgtcatttacgcatacttcaacaagg
actttcaaaacgcgtttaagaagatcattaagtgtaacttctgc**gcggccgcacggggacgcac**
cccacccagcctgggtccccaagatgagtcctgcaccaccgccagctcctccctggccaaggac
acttcatcgtga
(SEQ ID No. 12)

REPLACEMENT SHEET

FIGURE 11E

Nucleotide sequence of the β3AR-V2R chimera

atggctccgtggcctcacgagaacagctctcttgccccatggccggacctccccaccctggcgc
ccaataccgccaacaccagtgggctgccaggggttccgtgggaggcggccctagccggggccct
gctggcgctggcggtgctggccaccgtgggaggcaacctgctggtcatcgtggccatcgcctgg
actccgagactccagaccatgaccaacgtgttcgtgacttcgctggccgcagccgacctggtga
tgggactcctggtggtgccgccggcggccaccttggcgctgactggccactggccgttgggcgc
cactggctgcgagctgtggacctcggtggacgtgctgtgtgtgaccgccagcatcgaaaccctg
tgcgccctggccgtggaccgctacctggctgtgaccaacccgctgcgttacggcgcactggtca
ccaagcgctgcgcccggacagctgtggtcctggtgtgggtcgtgtcggccgcggtgtcgtttgc
gcccatcatgagccagtggtggcgcgtaggggccgacgccgaggcgcagcgctgccactccaac
ccgcgctgctgtgccttcgcctccaacatgccctacgtgctgctgtcctcctccgtctccttct
accttcctcttctcgtgatgctcttcgtctacgcgcgggttttcgtggtggctacgcgccagct
gcgcttgctgcgcggggagctgggccgctttccgcccgaggagtctccgccggcgccgtcgcgc
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ggcccgcgcgcctcctgcctctccgggaacaccgggccctgtgcaccttgggtctcatcatggg
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tctctagtcccgggcccggctttccttgccctgaactggctaggttatgccaattctgccttca
acccgctcatctactgccgcagcccggactttcgcagcgccttccgccgtcttctgtgccgctg
cgcggccgcacggggacgcaccccacccagcctgggtccccaagatgagtcctgcaccaccgcca
gctcctccctggccaaggacacttcatcgtga
(SEQ ID No. 13)

FIGURE 11F

Nucleotide sequence of the Edg1-V2R chimera

atggggcccaccagcgtcccgctggtcaaggcccaccgcagctcggtctctgactacgtcaact
atgatatcatcgtccggcattacaactacacgggaaagctgaatatcagcgcggacaaggagaa
cagcattaaactgacctcggtggtgttcattctcatctgctgctttatcatcctggagaacatc
tttgtcttgctgaccatttggaaaaccaagaaattccaccgacccatgtactattttattggca
atctggccctctcagacctgttggcaggagtagcctacacagctaacctgctcttgtctggggc
caccacctacaagctcactcccgcccagtggtttctgcgggaagggagtatgtttgtggccctg
tcagcctccgtgttcagtctcctcgccatcgccattgagcgctatatcacaatgctgaaaatga
aactccacaacgggagcaataacttccgcctcttcctgctaatcagcgcctgctgggtcatctc
cctcatcctgggtggcctgcctatcatgggctggaactgcatcagtgcgctgtccagctgctcc
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tgctctccatcgtcattctgtactgcagaatctactccttggtcaggactcggagccgccgcct
gacgttccgcaagaacatttccaaggccagccgcagctctgagaagtcgctggcgctgctcaag
accgtaattatcgtcctgagcgtcttcatcgcctgctgggcaccgctcttcatcctgctcctgc
tggatgtgggctgcaaggtgaagacctgtgacatcctcttcagagcggagtacttcctggtgtt
agctgtgctcaactccggcaccaaccccatcatttacactctgaccaacaaggagatgcgtcgg
gccttcatccggatcatgtcctgctgcaagtgc**gcggccgcacggggacgcaccccacccagcc**
tgggtccccaagatgagtcctgcaccaccgccagctcctccctggccaaggacacttcatcgtg
a
(SEQ ID No. 14)